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Applicants:	Darrell H. Carney, Roger S. Crowther, David J. Simmons, Jinping Yang and William Redin		
Application No.:	09/909,122	Group Art Unit:	1647
Filed:	July 19, 2001	Examiner:	DeBerry, R.M.
Confirmation No.:	1024		
For:	STIMULATION OF BONE GROWTH WITH THROMBIN PEPTIDE DERIVATIVES		

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or is being facsimile transmitted to the United States Patent and Trademark Office on:

12-31-03 Dawn M Myers
Date Signature

Dawn M Myers
Typed or printed name of person signing certificate

DECLARATION OF DARRELL H. CARNEY, PH.D.
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Darrell H. Carney, Ph.D., of 1125 Tallow Drive, Dickinson, Texas 77539, U.S.A., declare and state that:

1. I am one of the inventors of the subject matter described and claimed in U.S. Application No. 09/909,122 ('122), filed July 19, 2001.

2. I have been on the faculty at the University of Texas Medical Branch, 301 University Boulevard, Galveston, Texas 77555, U.S.A. since 1978, most recently as a Professor and Vice Chairman in the Department of Human Biological Chemistry and Genetics. I am also founder, President and Chief Executive Officer of Chrysalis BioTechnology Inc., 220 Market Street, Suite 605, Galveston, Texas 77550, U.S.A. A copy of my curriculum vitae, which describes my educational and professional experience, is attached as Exhibit A.

I have published extensively in refereed publications, most of which have focused on the role of thrombin, thrombin peptides and thrombin receptors in cellular regulation. A list of publications authored or co-authored by me is included as part of my curriculum vitae.

3. I have found that ***osteoblasts have high-affinity thrombin receptors and respond to compounds such as TP508 which activate the non-proteolytic thrombin cell surface receptor (NPAR)*** but do not have proteolytic activity to activate the proteolytically activated receptors (PAR1-PAR4). I have also found that ***compounds that activate NPAR stimulate osteoblast proliferation***.

The following is a description and discussion of the experimentation performed by me or under my supervision and of the results which demonstrate that osteoblasts have high-affinity thrombin receptors and respond to NPAR agonists resulting in the stimulation of osteoblast proliferation.

Thrombin Binding to Mouse Osteoblasts

The specific binding of ^{125}I thrombin to MC3T3-E1 (subclone 4) osteoblasts (ATCC No. CRL-2593) was carried out using established thrombin receptor binding assays as disclosed in U.S. Patent No. 5,352,664 and Carney, D.H. and Cunningham, D.D., *Cell*, 15:1341-1349 (1978). Briefly, highly purified thrombin was iodinated and added to cultures of osteoblasts with or without unlabeled thrombin to correct for nonspecific binding. By incubating cells with different concentrations of labeled thrombin and measuring the amount

of thrombin bound to cells and the amount of free thrombin in the medium, it is possible to estimate the number of receptors per cell and the affinity of thrombin for that binding site.

Scatchard analysis of labeled thrombin binding from two separate experiments indicate that mouse MC-3T3 osteoblasts have two classes of high-affinity receptors on their cell surfaces with an average of 83,000 very high affinity binding sites per cell (Kd = ~230 pM) and 180,000 high affinity sites (Kd = ~16.8 nM). This binding is similar to that reported for high-affinity thrombin binding to fibroblasts (Carney, D.H. and Cunningham, D.D., *Cell*, 15:1341-1349 (1978)), and for which TP508 competes for binding (U.S. Patent No. 5,352,664 and Glenn, K.C. *et al.*, *J. Peptide Research*, 1:65-73 (1989)) to initiate proliferative signals.

NPAR Agonist Stimulation of Mouse Osteoblast Proliferation

To determine the effect of NPAR agonists on osteoblast proliferation, MC3T3-E1 (subclone 4) osteoblasts (ATCC No. CRL-2593) were seeded into 24 well plates at a density of 5.0×10^4 cells per well and were cultured in DMEM with 10% fetal calf serum. After 24 hours, the medium was removed and non-adherent cells were removed by rinsing the cultures gently with 1 ml of serum free DMEM (0% serum) and replacing the medium with 1 ml of DMEM. After 48 hours in serum free medium, the NPAR agonist TP508 (SEQ ID NO: 5) was added at the indicated concentrations from 0 to 100 μg per ml (Tables 1 and 2) and cell number was determined 48 hours later using a Coulter Cell Counter as described in Carney, D.H. and Cunningham, D.D., *Cell*, 15:1341-1349 (1978). As shown in Tables 1 and 2, addition of TP508 increased cell number in two separate experiments relative to that seen in untreated control osteoblasts (0 μg) by approximately 20%. The results from the two experiments are also shown in Figure 1.

Table 1: Experiment 1

Treatment	Cell Number (cells/well) ± SD
TP508 (0 μg)	39696.7 ± 3266.1
TP508 (10 μg)	44500.0 ± 4217.1
TP508 (30 μg)	46420.0 ± 2271.1
TP508 (100 μg)	48306.7 ± 1804.9

Table 2: Experiment 2

Treatment	Cell Number (cells/well) ± SD
TP508 (0 μg)	43070.0 ± 2358.5
TP508 (10 μg)	44906.7 ± 1026.9
TP508 (30 μg)	46493.3 ± 3890.5
TP508 (100 μg)	47380.0 ± 698.7

4. The subject application (the '122 application) discloses results which demonstrate that compounds which activate NPAR are osteoinductive. The application discloses results which demonstrate that NPAR agonists can stimulate bone growth at a site within a subject at which bone growth would not occur if the site were left untreated. In particular, the application discloses results which demonstrate that TP508 is osteoinductive and induces bone formation in sites where bone formation did not occur without treatment (see, e.g., Examples 1 and 2).

5. U.S. Patent No. 5,352,664 ('664) and U.S. Patent No. 5,500,412 ('412) (copies of which are attached hereto as Exhibits B and C), of which I am an inventor of the subject matter described and claimed therein, set forth experiments and results which demonstrated that epithelial cells and fibroblast cells have high-affinity thrombin receptors and that thrombin peptide derivatives (NPAR agonists), including TP508, can bind specifically to the thrombin receptors (see Example 4). These earlier applications also disclose results which

demonstrated that NPAR agonists, including TP508, acting on the thrombin receptors, can induce DNA synthesis and promote proliferation of these cells (see Example 5).

6. The '664 and '412 patents demonstrated that: (1) NPAR receptors are present on epithelial cells and fibroblast cells; and (2) activation of NPAR receptors by agonists, such as TP508, stimulate proliferation of these cells.

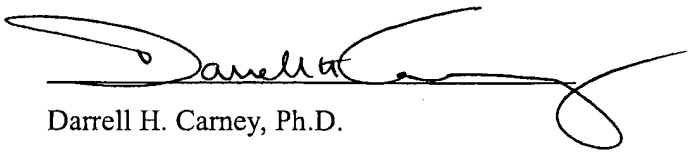
The results described herein in paragraph 3 provide evidence showing that: (1) NPAR receptors are present on osteoblasts; and (2) TP508 stimulates osteoblasts to proliferate. The subject ('122) application provides evidence showing that TP508 is osteoinductive, stimulating bone formation in sites where bone formation did not occur without treatment.

From the data, I conclude that activation of NPAR causes osteoblasts to proliferate. Therefore, agonists other than TP508, e.g., those which act on epithelial and fibroblast cells, would also cause osteoblast proliferation. I conclude that NPAR agonists other than TP508 would be osteoinductive and stimulate bone formation in sites where bone formation would not occur without treatment. I further conclude that analogs of TP508, such as those recited in claims of the '664 and '412 patents, would stimulate osteoblast proliferation. I also conclude that analogs of TP508 such as those recited in claims of the '664 and '412 patents are expected to be osteoinductive, stimulating bone formation at sites where osteoinduction is needed (i.e., at sites where bone formation would not occur if the sites were left untreated).

7. Since analogs of TP508 have been shown to activate NPAR, analogs of TP508 would also be expected to stimulate osteoblasts, given the evidence that NPAR receptors are present on osteoblasts and TP508 stimulates osteoblasts to proliferate. Thus, I conclude that analogs of TP508 would stimulate osteoblast proliferation, and be osteoinductive, stimulating bone formation at sites where osteoinduction is needed (i.e., at sites where bone formation would not occur if the sites were left untreated).

8. I declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true.

Moreover, these statements are made with the knowledge that willful false statements and the like made by me are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Darrell H. Carney, Ph.D.

December 30, 2003

Date

Attachments

Exhibit A	Curriculum vitae, including list of publications
Exhibit B	U.S. Patent No. 5,352,664 ('664)
Exhibit C	U.S. Patent No. 5,500,412 ('412)

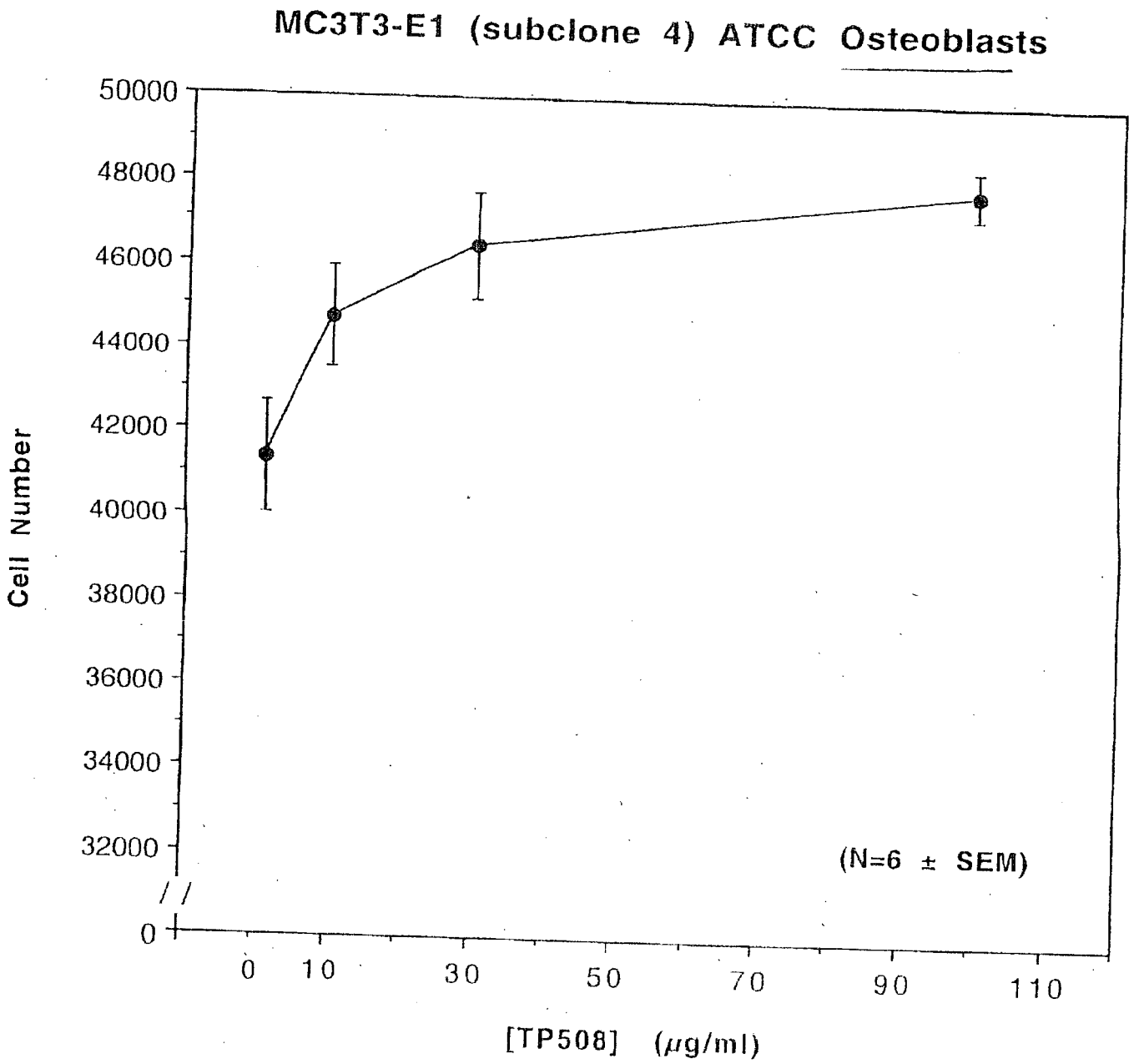

MC3T3-E1 (subclone 4) ATCC Osteoblasts
50000
48000
46000
44000
42000
40000
38000
36000
34000
32000
0
Cell Number
0
10
30
50
70
90
110
[TP508] (μg/ml)
(N=6 ± SEM)

FIG. 1

CURRICULUM VITAE

NAME: **Darrell Howard Carney** DATE: January 1, 2003

PRESENT POSITION AND ADDRESS:

Professor and Vice Chairman (September 2000)
Department of Human Biological Chemistry and Genetics
The University of Texas Medical Branch
Galveston, TX 77555-0645
(August, 1978)
Phone: (409) 772-3210
Fax: (409) 772-2348
Email: dcarney@utmb.edu

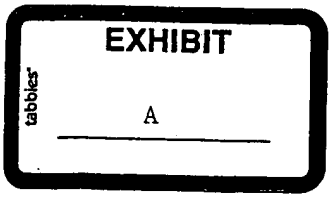
Chrysalis BioTechnology, Inc. (November 1995)
2200 Market, Suite 600
Galveston, TX 77550
Phone: (409) 750-9251
Fax: (409) 750-9253
Email: dcarney@chrysalisbio.com

BIOGRAPHICAL:

Date and Place of Birth:	April 15, 1948, Boise, Idaho
Citizenship:	USA
Social Security Number:	518-52-7622
Home Address:	1125 Tallow Drive Dickinson, Texas 77539
Phone:	(281) 534-3276
Fax:	(281) 337-4832

EDUCATION:

Institution	Date	Major	Degree
Northwestern University Evanston, Illinois	1966-68	Biology	
College of Idaho Caldwell, Idaho	1968-70	Biology	B.S.
University of Connecticut Storrs, Connecticut	1970-75	Developmental Biology	Ph.D.
University of California Irvine, California	1975-78	Cell Biology	Postdoctoral



PROFESSIONAL AND TEACHING EXPERIENCE:

1971-1972	Teaching Assistant in Developmental Biology and Human Anatomy, University of Connecticut
1972-1975	NIH Predoctoral Trainee Cell Biology Training Grant - GM 00317
1975-1978	NIH Postdoctoral Fellowship University of California, Irvine - CA 12306
1976-1978	Instructor in Medical Microbiology University of California, Irvine
1978-1982	Assistant Professor, Biochemistry Division, Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch, Galveston, TX (August 1978)
1978-Pres.	Biochemistry Program, Graduate School of Biomedical Sciences The University of Texas Medical Branch, Galveston, TX (August 1978)
1982-1992	Associate Professor, Division of Biochemistry The University of Texas Medical Branch, Galveston, TX (September 1982)
1986-1998.	Director of UTMB Peptide-DNA Synthesis Laboratory The University of Texas Medical Branch, Galveston, TX
1987-1988	Co-Director, UTMB Cancer Center Program; Hormone-Receptor Interactions in Cancer. The University of Texas Medical Branch, Galveston, TX
1992-Pres	Professor, Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch, Galveston, TX (September 1992)
1994-1995	Founder, Gal Tech Wound Therapies, DBA. 201 University Blvd. Suite 924, Galveston, TX (July, 1994)
1995-Pres	Founder and Scientific Director, Chrysalis BioTechnology, Inc. 2200 Market, Suite 600, Galveston, TX 77550 (November, 1995)
1997-Pres	President and CEO, Chrysalis BioTechnology, Inc. 2200 Market, Suite 600, Galveston, TX 77550 (July, 1997)
1998-Pres	Partner, Emprise Scientific, DBA of Emprise Partners, LTD. 1125 Tallow Drive, Dickinson, TX 77539 (July 1998)
2000-Pres	Vice Chairman, Department of Human Biological Chemistry & Genetics, UTMB. (September, 2000)

RESEARCH ACTIVITIES:

1968-1970 Undergraduate, College of Idaho, Biology Department
Independent Research, Funded by the Idaho Heart Association.

1970-1975 Graduate Research, University of Connecticut, Storrs, Connecticut. Departments of Animal Genetics and Genetics and Cell Biology, Norman W. Klein, Advisor. Biochemistry and Developmental Biology of brain development.

1975-1978 Postdoctoral Research, The University of California, Irvine, Department of Medical Microbiology,
Dennis D. Cunningham, Advisor Regulation of cell proliferation. Studies led to discovery and identification of thrombin receptors on the surface of fibroblasts and other cells.

1978-Pres. The University of Texas Medical Branch, Department of Human Biological Chemistry and Genetics. Role of thrombin receptors and thrombin-derived peptides in regulating cellular activities as they relate to inflammation, tissue repair, and cancer.

Based on our initial discovery of thrombin receptors on cells, our laboratories have studied the activation of these receptors and the subsequent signal cascades initiated by proteolytic and non-proteolytic thrombin interactions with cells. These studies have demonstrated that thrombin interacts with and activates a non-proteolytically activated thrombin receptor (NPAR) that is distinct from the proteolytically activated receptors (PAR1-4). Using synthetic peptides we identified the high-affinity binding domain of thrombin and discovered that the thrombin peptide TP508, representing this domain, activates NPAR and stimulates specific cellular activities that accelerate tissue repair. This peptide, also known as Chrysalin®, has been tested in Phase II safety and efficacy human clinical trials for accelerating the healing of chronic diabetic ulcers and orthopedic (distal radius) fractures. Based on positive results from these first trials, Phase II (diabetic ulcer) and Phase III (fresh fracture) trials will be initiated in 2002 by Chrysalis BioTechnology and its strategic partners Abbott Laboratories and OrthoLogic. In addition, human clinical trials to test the efficacy of thrombin peptides in spine fusion, cartilage repair, and myocardial revascularization are planned for initiation in 2002.

Because TP508 is proving to be an effective and potentially important molecule for orthobiologics, dermal tissue repair, prevention of vascular restenosis and revascularization of ischemic heart, basic science studies in our laboratory and in the laboratories of our collaborators are focusing on: (i) understanding the signal transduction pathways stimulated by activation of the non-proteolytically activated thrombin receptor (NPAR) in different tissues using array analysis and other techniques; (ii) cloning the NPAR receptor; (iii) and developing validated cell assays to screen peptide analogues and mimetics for activity.

RESEARCH SUPPORT

A. Previous Support

1978-79	Institutional Biomedical Research Support Grant DHEW 5-S07RR05427	$ 7,200
1978-79	Cancer Center Core Grant (CA 17701-04) "Thrombin Receptors in Normal and Transformed Cells"	8,750
1978-79	American Cancer Society Institutional Research Grant No. IN 112B	2,950
1979-80	UTMB Cancer Center - "Video Intensification of Cell Surface Molecules"	17,000
1979-82	DHEW 1R0l-AM-25807, (01-03) "Role of Cell Surface in Regulating Cell Proliferation."	164,307
1982-87	DHHS 1 K04 CA00805, (01-05) Research Career Development Award	190,050
1982-87	DHHS 2R01 AM 25807, (04-08) "Role of Cell Surface in Regulating Cell Proliferation"	380,869
1983	Intramural Grant "Microinjection of Macromolecules into Single Living Cells."	21,500
1984-85	NSF PMC-8400954 "Acquisition of a Gas-Phase Protein Sequencer" (Co-P.I.)	65,000
1984-88	DHHS 1R01 GM 33505 "Studies of Cytoplasmic Microtubule Heterogeneity" (Co-investigator, 5% effort)	228,662
1985-86	Texas Neurofibromatosis Foundation, "Autocrine Stimulation of Neurofibromatosis by Growth Factors or Their Receptors."	9,091
1986-88	UTMB Administrative Support Grant, "Peptide and Oligonucleotide Synthesis Laboratory"	180,000
1987-88	DRR-BRS 1-S10RR03469, Principle Investigator "UTMB Peptide Synthesizer Facility"	95,500
1987-1997	UTMB Administrative Yearly Support Grant, "Peptide and Oligonucleotide Synthesis Laboratory"	30,000
1988-89	Monsanto Co./Searle, "Thrombin Peptides as Biological Response Modifiers"	40,000

1988-90	Texas Advanced Technology Program, "Thrombin and Synthetic Peptides in Wound Healing and Modulation of Biological Responses"	178,490
1989-92	Texas Advanced Technology Program, P. I., "Thrombin Peptides as Enhancers of Tissue and Bone Healing, and Inhibitors of Adhesions and Vascular Permeability"	200,000
1989-92	J. D. Searle. "Preclinical Evaluation of Thrombin Peptides as Enhancers of Wound Healing"	60,000
1987-93	DHHS 2R01 DK 25807 (09-15), "Role of Cell Surface in Regulation of Proliferation"	736,227
1992-94	American Diabetes Association, "Possible Acceleration of Diabetic Wound Healing with Thrombin and Synthetic Thrombin Receptor Activating Peptides"	79,941
1992-95	Johnson & Johnson Medical Inc., "Evaluation of Immobilized-TRAP-508 as a Wound Healing Device	43,976
1993-98	RO1-GM47572 "Role of Thrombin Peptides in Regulating Wound Healing." (P.I.) 5-years	591,950
1995	1 R43 AI38153-01 "Thrombin Peptide Effect on Cellular Antimicrobial Action" (Co Investigator, J. Stiernberg, Ph.D., P. I.)	100,000
1997-01	NIH 1R44-AI-38153 SBIR Phase II grant "Antimicrobial action of TRAP-508 (DHC, Co-Investigator, Janet Stiernberg, Ph.D., PI)	$750,000
1999-01	NIH-SBIR Phase I grant "Accelerated Fracture Repair Using Thrombin Peptides" (DHC-Scientific Director, Roger Crowther, PI)	$100,000
1997-01	NIH 1R44-DK 53580 SBIR Phase I/Phase II " Effect of Thrombin Peptides on Chronic Wounds" (DHC-Scientific Director, Laurie Sower, Ph.D., PI)	$850,000
1999-01	1 R 43 HL64508-01 NIH-SBIR Phase I Grant (A Norfleet, PI) "Inhibition of vascular restenosis by the TP508 peptide" (DHC-Scientific Director, Co-investigator)	$100,000
1999-01	1 R 43 AR46343-01 NIH-SBIR Phase I Grant (J. Stiernberg, PI) Cartilage repair induced by thrombin peptide TP508 (DHC-Scientific Director, Co-investigator)	$100,000

B. Current Support

D. H. Carney, Principal Investigator

1999-2003 CHR-001 "Molecular Mechanisms of Thrombin in Wound Healing, Inflammation, and Vascular Repair" Chrysalis BioTechnology, Inc. (P.I.) 800,000

D. H. Carney, Co-PI/Co-Investigator

1999-02 1R 44 AR 45508-02 NIH-SBIR Phase II Grant $750,000
"Accelerated Bone Repair by a Synthetic Thrombin-Derived Peptide" (DHC-Scientific Director, Roger Crowther, PI)

2001-02 1R 43 HL69661-01 NIH-SBIR Phase I Grant $100,000
"Revascularization of Ischemic Heart Tissue by TP508" (DHC- Co-Investigatior, Chris Coleman, PI)

C. Pending Support

1 R 44 HL64508-02 NIH-SBIR Phase II Grant (C. Coleman, PI)
"Inhibition of vascular restenosis by the TP508 peptide"
(DHC-Scientific Director, Co-investigator) $750,000

1 R 44 NIH SBIR Phase I Grant (M. Keherly, PI) entitled "Enhanced Antimicrobial Activity by Synthetic Peptide NTP"
(DHC, Co-investigator) $100,000

D. Patent Applications / Inventions

1986 "Thrombin Polypeptides :Composition and Methods for Use", **Darrell H. Carney** and Kevin C. Glenn, US. Patent Issued (5, 925,201) October 4, 1994. Issued, 10/04/94 Patent No 5,352,664.

1987 "Thrombin Peptides which Modulate Receptor Occupany and Mitogenic Stimulation", **Darrell H. Carney** and Kevin C. Glenn.
European Patents 87 907 652.9-2110 (US87/02882), Issued.

1986 "Use of a Radiolabeled Monoclonal or Monovalent F(ab) Fragments of Monoclonal Antibodies for Quantitation of Cytoskeletal Antigens" (Invention Disclosure), WC Thompson, **DH Carney** and RL Ball.

1994 "Thrombin Peptides which Modulate Receptor Occupancy and Mitogenic Stimulation", Divisional Application for Use in Wound Healing. **Darrell H. Carney** and Kevin C. Glenn (#UTSG-043),
Div. of (5, 925,201). US. Patent Issued Number 5, 500,412, March 19,1996.

1994 "Synthetic Peptide Neutrophil Cell Chemotactic Agents" **Darrell H. Carney** and Shyam Ramakrishnan (Disclosed to UTMB August, 1994), Patent Application 08/330,594 filed October 28,1994 (DC-006) by Chrysalis BioTechnology, Issued 10/30/01.

1995 "Thrombin Polypeptides: Composition and Methods for Use", **Darrell H. Carney** and Kevin C. Glenn, Divisional application for anti metastatic and inhibitory use of thrombin peptides to prevent unwanted proliferation or alteration of cellular function. (Pending).

2000 "Thrombin Derived Polypeptides: Compositions and Methods for Use. **Carney, D.H.** and Glenn, KC. Divisional Application #3033.1001-003 filed 8/02/00

2000 "Thrombin Derived Polypeptides: Compositions and Methods for Use. **Carney, D.H.** and Glenn, KC. Divisional Application #3033.1001-004 filed 8/02/00

2000 "Method of therapy with Thrombin Derived Peptides" **Carney, D.H.** Provisional Application for use of thrombin peptides in cardiovascular repair, inhibition of restenosis and myocardial revascularization. #3033.1000-000 Filed 07/12/00.

2000 "Stimulation of Bone Growth with thrombin peptide derivatives" **Carney, DH.**, Crowther, R., Simons, D., Redin, WR., Yang,J. Provisional application for use of thrombin peptides in repair of bone segmental gap filling, spinal fusion and areas where new bone growth are required. #3033.1002-000 Filed 7/19/00.

2000 "Stimulation of Cartilage Growth with agonists of the non-proteolytically activated thrombin receptor. **Carney, D.H.,** Crowther, R., Stiernberg, J., and Bergmann, J. Provisional application for use of thrombin peptides in cartilage and ligament repair, disc repair, etc. # 3033.1003-000 (60/219.800) filed 7/20/00.

2001 "Synthetic Peptide Neutrophil Cell Chemotactic Agents" **Darrell H. Carney** and Shyam Ramakrishnan (Continuation in part) filed June 2001

2001 "Method of therapy with Thrombin Derived Peptides" **Carney, D.H.** US, European PCT, Tiawan, and Thialand Applications for use of thrombin peptides in cardiovascular repair, inhibition of restenosis, and myocardial revascularization. #3033.1000-000. Filed on 07/12/01.

2001 "Stimulation of Bone Growth with thrombin peptide derivatives" **Carney, DH.**, Crowther, R., Simons, D., Redin, WR., Yang,J. US and European PCT application s for use of thrombin peptides in repair of bone segmental gap filling, spinal fusion and areas where new bone growth is required. #3033.1002-000. Filed on 7/19/01.

2001 "Stimulation of Cartilage Growth with agonists of the non-proteolytically activated thrombin receptor. **Carney, D.H.**, Crowther, R., Stiernberg, J., and Bergmann, J. US and European PCT for use of thrombin peptides in

cartilage and ligament repair, disc repair, etc. # 3033.1003-000 (60/219.800) filed 7/20/01.

2001 "Method for promoting healing of diabetic ulcers." **Carney, D.H.,** Provisional US Application based on results of human diabetic ulcer trials. #3033.1008-000. Filed on 7/27/2001.

COMMITTEE RESPONSIBILITIES

A. National Committees/Editorial Advisory Boards/Manuscript Reviews, Etc.

1978-Pres.	Ad Hoc Reviewer of Manuscripts for: J. Biol. Chem., J. Cell. Biochem., J. Cell Biology, J. Cell. Physiol., J. Clin. Invest., FASEB Journal, Cancer Research, Lab. Investigation, Molecular Endocrinology, Nature, Federation Proceedings, Biochem. J., J. Pharmacological Res., Cell Motility and Cytoskelton, and National Science Foundation Grants.
1982	National Institute of Allergy and Infectious Diseases, Transplantation Biology and Immunology, Subcommittee (Program Project Study Section) (Ad Hoc Member)
1986	Neurological Sciences 1 Ad Hoc-2 Study Section
1986-90	Editorial Advisory Board, Molecular Endocrinology
1989	National Heart, Lung and Blood Institute, Program Project Site Visit (Albany, NY).
1989	Oklahoma Center for the Advancement of Science and Technology, Member, Study Section, (March, 19-21).
1989	Oklahoma Center for the Advancement of Science and Technology, Chair, Biomedicine/Biotechnology Study Section, (October 15-17).
1989-91	Consultant, J.D. Searle and Co., Wound Healing Agents.
1990	Oklahoma Center for the Advancement of Science and Technology, Chair of Chairs, Biomedicine/Biotechnology Study Session, (Feb. 18-20).
1991	Oklahoma Center for the Advancement of Science and Technology, Biomedicine - Biotechnology Study Session, (February)
1991-1997.	Consultant, Oklahoma Center for Advancement of Science and Technology
1992	NIH Clinical Sciences Study Section, subcommittee.
1994	NIH GM Special Study Section, Chronic Wound Healing.
1994-1995	Founder and Scientific Director, Gal Tech Wound Therapies.
1995-Pres.	Founder and Scientific Director, Chrysalis BioTechnology, Inc.
1998-99.	Wound Healing Society Program Committee

B. UTMB Committees

1. Graduate School of Biomedical Sciences Committees

1980-1988 Graduate Program Review Committee
1981 Vice-Chairman
1982-1988 Chairman
1988-1996 Scholarship Committee.
1992-1996 Chairman
1992-1996 Graduate Recruitment Committee

Advancement to Candidacy, Examination Committees

1979	Randall Kohl	Biochemistry
1980	John Scott Somerset	Genetics & Cell Biology
1980	Helena Hwu	Biochemistry
1980	Kathryn L. Crossin	Biochemistry
1981	Craig S. Woodard	Genetics & Cell Biology
1982	Gregory R. Alsip	Genetics & Cell Biology
1983	Rampyari Raja	Biochemistry
1983	Robin Cooper	Genetics & Cell Biology
1984	Gloria Frost	Biochemistry
1985	Hillary Heard	Microbiology
1985	Eve Johnson	Microbiology
1985	Jonathan Lloyd	Anatomy
1986	Eric Gordon	Biochemistry
1986	Gulzar Sandhu	Biochemistry
1986	Jonathan Lloyd	Anatomy
1987	Jerome Choate	Neuroscience
1989	Olapade James	Biochemistry
1990	Shyam Ramakrishnan	Biochemistry
1990	David Scott	Genetics & Cell Biology
1992	Dennis Kim	Biochemistry, Genetics & Cell Biology
1992	David Millinoff	Microbiology
1994	Laurie Sower	Microbiology
1996	David Hester	HBC & G
1997	Christie Bogolin	HBC & G

Masters Degree Supervisory Committees

1981-1982 M. Sheila Trumble, Pathology
1981-1983 Rebecca Ball, Microbiology
1988-1988 Nora Davis, Biochemistry, Supervisor
1989-1990 Fang Wang, Genetics & Cell Biology, Supervisor
1992-1992 Vanessa Paulley, Biochemistry, Genetics & Cell Biology, Supervisor

Ph.D. Supervisory Committees

1979-1980 John M. Nickerson, Genetics & Cell Biology
1980-1982 Kathryn L. Crossin, Biochemistry, Supervisory Professor,
1982-1984 Janet Stiernberg, Biochemistry, Research Supervisor
1982-1986 Robin Cooper, Cell Biology
1982-1986 Gregory R. Alsip, Genetics & Cell Biology
1984-1986 Rampyari Raja, Biochemistry

1982-1987	Hillary Heard, Microbiology
1983-1987	Rebecca Ball, Microbiology, Research Supervisor
1984-1987	Debra Morris, Preventive Medicine and Community Health, Research Supervisor
1985-1987	Sang-Uk Nham, Human Genetics & Cell Biology
1985-1991	Stephen Pearson, Biochemistry
1985-1988	Lawrence Smith, Microbiology
1986-1987	Gloria Herbosa, Biochemistry, Supervisory Professor
1986-1989	Eve Johnson, Microbiology
1986-1989	Eric Gordon, Biochemistry, Supervisory Professor
1987-1987	Johnathan Lloyd, Anatomy
1987-1990	Jerome Choate, Neuroscience
1988-1991	Alexandra Kemendy, Physiol & Biophys
1990-1995	David L. Scott, Human Genetics & Cell Biology, M.D./Ph.D. Program. S. Professor
1991-1994	Olapade James, Biochemistry, Genetics & Cell Biology, Supervisory Professor.
1992-1994	Shyam Ramakrishnan, Biochem Genetics & Cell Biology, Supervisory Professor.
1992-1994	Dennis Kim, Biochemistry, Genetics & Cell Biology, M.D./Ph.D. Program. Supervisory Professor.
1994-1995	Laurie Sower, Microbiology.
1994-1995	Juan Yu, Neurobiology.
1997- 1999	BoJoy Yohanna, Microbiology
1997-1999	Kevin Bobbitt, Microbiology

2. School of Medicine Committees
   a. Past Committee Service

1981	Search Committee to select Chairman of Radiation - Cancer Therapy Department
1981	Search-Advisory Committee to select Director of Academic Computing and Biostatistics
1982-1983	Academic External Review Committee to review the Department of Anatomy
1983	Academic External Review Committee to review the Department of Microbiology
1984-1985	Faculty Advisory Committee, National Student Research Forum
1986	Search Committee to select Dean of the Graduate School and Research Vice-President
1987	External Review Panel to review the Department of Pharmacology
1987-1990	Elected Member of the Academic Planning Committee
1991	LCME Subcommittee for Self Study and Accreditation
1991-1993	Elected Member, Faculty Coordinating Council
1991-1993	Chair, Faculty Coordinating Council
1991-1993	Voting Member, Executive Committee of the Faculty of Medicine
1992-1993	Member Search Committee, Vice President for Public Relations and External Affairs
1984-1993	Intellectual Properties Committee (Patent Review Committee)
1986-1993	Chairman, Intellectual Properties Committee
1990-1993	Faculty Advisory Council -- Dean of Medicine
1989-1996	Advisory Committee for Continuing Medical Education
1995-1996	Nominating Committee

1996-1999. Technology Advisory Committee
1997-1999 Curriculum Committee Task Force - Dermal/Wound healing

b. Current Committee Responsibilities

3. Departmental Committees
a. Past Departmental Committee Service

1979 - 1985 Admission and Graduate Recruitment Committee - Biochemistry
1979 - 1990 Biochemistry Curriculum Committee
1982 - 1983 Departmental Travel Committee
1984 - 1990 Chairman, Biochemistry Credentials Committee
1986 - 1987 Departmental Recruitment Committee
1986 - 1988 Chairman's Advisory Committee
1989 - 1990 Departmental Recruitment Committee
1990 - 1992 HBC&G Graduate Program Credentials Committee
1991 - 1993 HBC&G Departmental Travel Committee
1991 - 1993 HBC&G Departmental Faculty Recruitment Committee
1993 - 1994 HBC&G Space Advisory Committee
1993 - 1995 Graduate Program Credentials Committee
1994 - 1997 Graduate Program Examination Committee
1995 - 1997 Chair, Graduate Program Exam. Committee
1995 - 1996 Chairman's Advisory Committee
1997-2000 Graduate Program Curriculum Committee

b. Current Departmental Committee Responsibilities

1998-Pres Compensation Advisory Committee
1999-Pres Chairman's Advisory Committee
1999-Pres Vice Chairman, Dept. of HBC&G
2000-Pres Department APT Committee

TEACHING RESPONSIBILITIES AT UTMB

A. Medical School

1987-1998 Medical Biochemistry, Cells and Genes 6501 - Lecture and SGSS on Cell Surface Receptors, Transport and Transmembrane Signals (five Lectures)

B. Graduate School

1979-1996 Biochemistry 6602 - Graduate Biochemistry Regulation and Control of Intermediary Metabolism (eight Lectures)

1979-1992 Biochemistry 6306 - Advanced Biochemistry Laboratory, Course Coordinator

1984-99 Fundamentals of Cell Biology 6407 - Receptor-Cytoskeletal Interaction, Transmembrane Signaling (4 lectures)

1991-97	HBC&G Special Topics, Growth Factors and Interleukins in Cellular Regulation. Course Co-coordinator (~20 hr of lecture, Course taught 1991, 92, 93, 95, 97).
1993- 1998	Cell Bio Program - Cell biology - Growth Factors and Cell Cycle Regulation (two lectures)
1993- 1996	Cell Bio Program- Biochemistry - "Energy and Intermediary Metabolism" and "Glycolysis" (two lectures)
1999 - present	BBSC Cell Biology 6204 Cell Cycle Regulation 4- lectures and/or one small group (alternating years).
2000-present	BBSC 6116 Inflammation Module, course co-director
2000-present	Cell Signaling Course, Co-director (~18 hours)

C. Current Graduate-Medical Students in Lab Training/Projects

none

D. Current Postdoctoral Fellows, Research Scientists, and Jr. Faculty

Janet Stiernberg, Ph.D.	Adjunct Assistant Professor in Human Biological Chemistry and Genetics, Successful PI on Wound Healing Project, NIH funded SBIR grants to study cellular antimicrobial activity of the thrombin peptide TP508 and its effect on chronic wound healing and cartilage repair.
Roger Crowther, Ph.D.	Adjuct Assistant Professor, Dr Crowther directs the Chrysalis BioTechnology Analytical Laboratory and oversees formulation and stability testing of TP508 products. PI on several Phase I/II SBIR NIH grants to study effects of TP508 in fresh fracture and other orthopedic applications.
Andrea Norfleet, Ph.D.	Preclinical Study Director. Dr. Norfleet is studying the mechanism of tissue repair stimulation by the TP508 peptide. Her initial projects involve identifying matrix and growth factor molecules that are stimulated early in tissue repair tissue by addition of TP508. In these studies she is using quantitative histology, immunocytochemistry, and *in situ* hybridization. She also obtained funding for a new SBIR project in vascular repair that demonstrated that TP508 may effectively reduce restenosis even in hypercholesterolemic rabbits.
Michael Kerheley, Ph.D.	Adjuct Assistant Professor, Group Director for BioDiscovery and Molecular Biology. Initial projects involve work on cloning the NPAR thrombin receptor and development of in vitro biological assays to test synthetic peptides for activity

related to tissue repair. Mike is also working on development of new technologies for tissue repair, modulation of infection and inflammation, and anti cancer applications

Mohammad Saeed Postdoctoral, BioDiscovery and Molecular Biology, focusing on receptor cloning projects. Recently, Mohammad has used the yeast-2 hybrid system to identify a family of proteins that bind to thrombin and thrombin peptides. He has also constructed expression vectors which can be tagged or expressed with GFP to study effects of TP508 expression in cells.

MEMBERSHIP IN SCIENTIFIC SOCIETIES:

American Society for Cell Biology
The Wound Healing Society
American Diabetes Association (professional)
European Academy of Science

HONORS:

Research Career Development Award, National Cancer Institute (1982-87).
Distinguished Alumni (Albertson College of Idaho, 1998).

ADDITIONAL INFORMATION

Invited Seminars, Symposia and Special Presentations

1978 "Proteases and Cell Proliferation." Panel Discussion ICN-UCLA Winter Symposium (March, Keystone, Colorado)

1980 "Relationship Between Cell Surface Receptors and Cytoplasmic Microtubules." International Symposium on Fundamental Mechanisms in Human Cancer Immunology. (Oct. 27, Galveston, TX).

1980 "Initiation of Cell Division by Thrombin-Receptor Interaction" UTMB Cancer Center Seminar Series (Sept. 16).

1981 "Surface Receptors and Cytoskeletal Interactions in Control of Normal and Neoplastic Cell Proliferation" UTMB Research Conference - Mini Symposium on Role of Cell Membranes in Control of Metabolism and Cell Behavior (June 23, Galveston, TX),

1981 "Preclustering of Thrombin Receptors and Their Interaction With Cytoplasmic Microtubules: Possible Role in Growth Regulation." Division of Endocrinology Research Seminar, The University of Texas Medical School at Houston (Houston, TX, Oct. 29).

1981 Chair, Platform Session on Receptor Mediated Endocytosis. American Society for Cell Biology (Nov. 10, Anaheim, California),

1982 "The Role of Microtubule Alterations in Initiation of DNA Synthesis" Federation of North Texas Area Universities 5th Annual Molecular Biology Symposium (May 21, Denton, Texas).

1982 "Role of Surface Receptors and Transmembrane Signaling in Initiation of Cell Proliferation" Department of Pharmacology Research Seminar, The University of Texas Medical Branch, Galveston, Texas, (Nov. 5)

1983 "Cell Surface, Receptors, Cytoskeleton and Receptor-Cytoskeletal Interactions." Two week lecture series - University of Puerto Rico, Rio Piedras, San Juan Puerto, Rico (Oct. 23-Nov. 1).

1984 "Mini symposia on Cellular Signal Transduction with Hormones, Mitogenesis and Oncogenes," American Society for Cell Biology (Nov. 13, Kansas City).

1984 "Microtubule Involvement in Initiation of Cell Proliferation" New York Academy of Sciences Conference on Dynamic Aspects of Microtubule Biology, (Dec. 3-6).

1985 "Thrombin Stimulated Phosphoinositide Metabolism Appears Necessary for Thrombin Mitogenesis," 69th Annual meeting of the Federation of American Societies for Experimental Biology, Anaheim, CA (April 21-26).

1985 "Double Lock Pathways Stimulated in Mitogenesis," Xth Congress of the International Society of Thrombosis and Haemostasis, San Diego, CA (July 15-18).

1985 "Role of Phosphoinositide Turnover in Thrombin Mitogenesis," 13th International Congress of Biochemistry -Amsterdam, The Netherlands (August 25-30).

1985 "Thrombin Receptor Occupancy Initiates Transient Increase in cAMP Levels in Mitogenically Responsive Hamster (NIL) Fibroblasts," New York Academy of Sciences, Conference on Bioregulatory Functions of Thrombin New York, NY (Feb. 5-7).

1985 Invited Seminar (International) "Thrombin receptors and transmembrane signals in regulation of cell proliferation" Centre de Biochimie, Seminar Program, Parc Valrose, Nice France (Sept. 1-4).

1986 International Workshop Organizer on Proteases and Biological Control. UCLA Symposium on Proteases, Park City, UT (Feb. 12).

1986 UTMB Representative, Special Conference on Academic-Industrial Interaction, Fisher Scientific Group, Hotel Del Coronado, San Diego, CA (July 10-13).

1986 "Modulation of Thrombin - Receptor Interaction in Cultured Neurofibroma and Neurosarcoma Cells," Texas Neurofibromatosis Foundation, Semi-annual meeting, Smithville, TX (Sept. 5).

1986 "Thrombin Peptide Interacts with High-Affinity Thrombin Receptors Initiating Part of the Proliferative Signal," Mini symposium on "Extracellular Proteases in Development and Neoplasia," at the 26th

Annual meeting of the American Society for Cell Biology, Washington, DC (Dec. 7-11).

1987 "Thrombin Stimulation of Proliferation: Role of Receptors, Cytoskeleton and Transmembrane Signals," Seminar-Department of Cell Biology and Anatomy, University of Alabama, Birmingham, AL (Feb. 18-20).

1988 "Thrombin Peptides Enhance Wound Closure and Increase Breaking Strength-Wound Healing Project Review." Monsanto Corporation Chesterfield, MO (March, 1988).

1988 "Mechanisms Involved in Thrombin Mitogenesis," Gordon Research Conference Speaker - Plymouth, NH (June 13-17).

1988 "Use of Synthetic Peptides as Probes for Receptor Ligand Interactions, Second Messenger Function and *in vivo* Modification of Biological Responses." Milligen Biosearch - National Frontiers in Molecular Biology Seminar Series.

1988 Invited Guest Speaker "Thrombin Receptors and Transmembrane Signals in Regulation of Cell Proliferation" Molecular Biology Seminar Series - University of Kansas, Lawrence KS (Feb. 3).

1989 "Thrombin and Synthetic Peptides in Wound Healing," Homecoming Address, The University of Texas Medical Branch, Galveston, TX (March 31).

1989 "Wound Healing Project Review - Research Alert." Monsanto Corporation, Chesterfield, MO (June 19-20).

1989 "Thrombin Peptides as Wound Healing Agents: Perspectives, Potential Efficacy, and Marketability," Monsanto Corporation - J.D. Searle and Company, Skokie, IL (August 30-31).

1990 "Thrombin and Thrombin Receptor Activating Peptides in Regulating Cell Proliferation *In Vitro and In Vivo*," University of Vermont Graduate Program Lecture Series in Cell and Molecular Biology, Burlington, VT (March 3-6).

1991 "Thrombin Peptides Promote Healing of Wounds in Steroid-Treated Rats." First International Meeting of the Wound Healing Society January 1991, Galveston, TX.

1991 "Synthetic Thrombin Peptides as Mediators of Cellular Processes *in vitro* and *in vivo*." Winter Neuropeptide Conference, Breckenridge CO, (February, 1991).

1991 "Postclotting Effects of Thrombin and Synthetic Thrombin Peptides: Potential Role in Wound Healing and Inflammation" Microbiology Seminar UTMB (May 1991).

1992 "Discovering Thrombin's Regulatory Diversity: Role of Thrombin and Thrombin Receptors in Cell Proliferation, Inflammatory Responses, and

Wound Healing." Faculty Research Colloquium: The University of Texas Medical Branch, (Jan. 27).

1992 "Research Update: Use of Synthetic Thrombin Peptides in Acceleration of Wound Healing." Johnson & Johnson Medical Inc., Dallas, TX (March 3-4).

1992 "Acceleration of Wound Healing and Thrombin Postclotting Cellular Activities *in vivo* using Synthetic Thrombin Receptor Activating Peptides" Somatix Therapy Corporation Seminar: Somatix Corp. Alameda CA. (April 24).

1992 "Role of Thrombin and Thrombin Receptors in Cell Proliferation, Inflammatory responses, and Wound Healing" Creative BioMolecules, Boston MA. (April 30).

1992 "Role of Thrombin and Synthetic Thrombin Receptor-Activating Peptides in Stimulation of Wound Healing, Inflammation, and Angiogenesis" Biogen Research Seminar, Boston, MA (August 6).

1992 "Stimulation of Wound Healing and Cellular Responses by Thrombin and Receptor Activating Thrombin Peptides" FASEB Conference on Structure and Function of Thrombin. Vermont (August 8-14).

1992 "Use of Synthetic Thrombin Peptides in Wound Healing." Research Update, Johnson & Johnson Medical Inc., Biopolymer Group, Stirling University, Stirling, U.K, (August 24).

1992 Delegate, 2nd European Tissue Repair Society Meeting, Malmo, Sweeden, (August 24-27). Johnson & Johnson Consultant

1993 Invited Research Seminar "Thrombin and Thrombin Peptides as Mediators of Inflammation and Tissue Repair" University of Houston, Biochemistry Department (March).

1993 State of the Art Lecture, "Role of Thrombin and Thrombin Peptides in Tissue Repair" International Congress of Thrombosis and Hemostasis, New York (July 3-12).

1993 "Efficacy of TRAP-508 in enhancing healing of incisional and open wounds in animal models" Spectrum Consumer Products, Houston TX (September 1993).

1994 "Effect of thrombin and thrombin peptides on corneal wound healing" Association for Research in vision and Ophthalmology, St. Petersburg Florida, (May 1994).

1994 Seminar, Thrombin Peptide Technology Update, Ventures Medical-Houston, TX (June 1994).

1994 Session Chair, "Thrombin and Cellular Systems" at the Fourth International Biennial Meeting on Blood Coagulation and Platelet Biology, "Thrombin functions and new Prospects in Antithrombotic therapy", Megeve, France, September 11-15, 1994.

1994 State of the Art Lecture, "Role of thrombin and thrombin peptides in initiation of inflammation and tissue repair" at the Fourth International Biennial Meeting on Blood Coagulation and Platelet Biology, Megeve, France, September 13, 1994.

1994 Invited International Seminar: "Role of thrombin and synthetic thrombin peptides in Inflammation and Wound Healing" University of Siena, Siena Italy, September 19, 1994

1995 Invited Seminar: "Effects of Thrombin and Synthetic Thrombin Peptides in Wound Healing" Cardiovascular Seminar Series, Sealy Center for Molecular Cardiology, UTMB, Galveston, TX.

1995 Discussant: FASEB Summer Conference on "Thrombin Structure and Function" Copper Mountain Colorado (August 1995).

1997 Seminar-Presentation: Thrombin peptides in wound healing. Biersdorf, AG, Hamburg, Germany, (January 10, 1997).

1997 Seminar-Presentations, "Thrombin Peptides in Wound Healing." Zurich Switzerland, Dr. Raphael Levi Feb. 13, 1997, and, Wuppertal, Germany, Bayer, AG. Feb. 14, 1997.

1997 Presentation, Bayer Biologics, New Haven, CT. "Thrombin and thrombin peptides in tissue repair" May 27, 1997.

1997 Presentation, US Surgical, New Haven CT., "Thrombin Peptide TP508 in soft and hard tissues: Potential therapeutic." May 28, 1997.

1997 Attendee: XVI Congress of the International Society on thrombosis and Haemostasis, Florence, Italy. June 4-11, 1997.

1997 Third FASEB Summer Conference on Thrombin, Saxon River Vermont. Meeting discussant - Presenter "Taking technology to market to support basic science research" August 9-13, 1997.

1997 Presentation: "Thrombin Peptide Use in Hard Tissue - Orthopedic Tissue Repair" OrthoLogic, Inc. Phoenix, AZ. October 13, 1997.

1997 Invited Seminar: Trinity University, SanAntonio, TX "Thrombin and Thrombin Peptides in Inflammation and Tissue Repair" Departments of Biology and Biochemistry October 20, 1997

1997 SBIR Workshop Presentation: "Opportunities to support basic science research using technology transfer and SBIR funding: Chrysalis BioTechnology, Inc. A Case Study" Universtiy of Texas Medical Branch health Science Center, Houston, TX. November 14, 1997.

1998 Keystone Winter Symposium, "Tissue Repair Mechanisms", Cooper Mountain, Colorado, January 10-14, 1998.

1998 Presentation to Drug Division, FDA "Use of Thrombin Peptide, TP508, in Surgical and Chronic Wound Healing, Pre-IND meeting. January, 20-21, 1998. Washington D.C.

1998 Invited Presentation. Arterial-Vascular Engineering (AVE), "Potential application of thrombin peptides for prevention of restenosis." January 29, 1998.

1998 Invited Presentation. Medtronic, Mineapolis Minn. "Potential application of thrombin peptides for prevention of restenosis." February 18, 1998.

1998 Invited Presentation. Medici Medical Technologies (The Edge Group), "Potential application of thrombin peptides for prevention of restenosis." February 20, 1998, Houston, TX.

1998 Invited Presentation. Guidant, San Francisco CA, "Potential application of thrombin peptides for prevention of restenosis." March 8-9, 1998.

1998 Seminar, UTMB Tissue Engineering Group, Pharmacology Conf. Rm., Synthetic peptides in Tissue Repair, Galveston, TX. March 10, 1998.

1998 OrthoLogic, Tempe, Arizona. "Use of Hyaluronic Acid as a vehicle for delivery of thrombin peptide, TP508." April 23, 1998.

1998 FDA presentation "Osteon" device for accelerated healing of fresh fracture. Presentation for device vs. drug determination for use of TP508 in orthopedic applications. April 29, 1998.

1998 Invited Seminar. "Use of TP508 for Interventional Cardiology" MIT, Cambridge Mass. Division of Cardiology. June 16, 1998.

1998 Wound Healing Society Annual Meeting, Oral Presentation. Thrombin peptide, TP508, stimulates wound healing through a non-proteolytic mechanism. Salt Lake City, Utah, June 20, 1998.

1998 OrthoLogic, Tempe, Arizona. Seminar, "Drug use of TP508 to accelerate fresh fracture healing." June 22, 1998.

1998 OrthoLogic, Tempe, Arizona. Meeting September 1, 1999

1998 Invited Cardiovascular Presentations, Guidant Corporation and AVE, September 9 and 10, 1998, California

1998 Invited Presentation, "Thrombin peptide TP508 use in soft and hard tissue repair." Trauma, Infection, and Repair Symposium, Galveston TX September 16,1998

1998 Invited Presentation, Washington DC "Effect of TP508 on neointima formation following angioplasty. AVE meeting with MIT collaborators. October 8,1998.

1998 Presentation and Discussions, UCSF. "Potential use of TP508 in spine fusion" November 12, 1998

1999 Invited Presentation. "New developments in Wound Healing with Chrysalin™ peptide TP508" 3M Corporation, Minneapolis, Minn. January 5, 1999.

1999 Invited Symposium Speaker Musculoskeletal Life Sciences Forum. "Tissue repair for the new millennium" Boston, Mass. January 27, 1999.

1999 Invited Presentation. "New developments in Wound Healing with Chrysalin™ peptide" Smith and Nephew, Tampa/St. Pettersburg, Florida. March 18, 1999.

1999 Invited Presentations (3). "New developments in Wound Healing with Chrysalin™ peptide" Baxter Hyland Immuno, Vienna Austria, Lohman Wound Care, Neuwied, Germany, and Smith Nephew, Hull, U.K. May 17-25, 1999.

1999 3rd Annual Biomaterials of the Future Conference, Medical Data International, SanFrancisco CA, "New advances in peptide technologies for repair of skin and bone" June 15, 1999.

1999 Symposium Speaker, Wound Healing Society, WOCN Joint Meeting and Educational Symposium, Therapeutic Possibilities for Problematic Wounds "Small Molecules for Wound Healing" Minneapolis Minn. June 20, 1999.

1999 Presentation to FDA, Washington DC, "Chrysalin™ for fracture healing in man" Pre-IND Meeting. July 15, 1999.

1999 Delegate, International Society for Thrombosis and Haemostasis Washington DC August 15-18,

1999 Attendee, Joint meeting of the European Tissue Repair Society and Wound Healing Society, Bordeaux France, August 24-28, 1999 .

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Hollister, Chicago Illinois (September 2, 1999).

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Healthpoint, San Antonio, TX (September 3, 1999)

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Baxter Immuno Group Vienna Austria (September 8, 1999).

1999 Workshop on "Effects of thrombin and thrombin peptides on inflammatory cells and cytokines" Rome, IT (September 9-10, 1999).

1999 Civic Presentation "The Good Aspects of BioTechnology: Advances in wound care and bio engineering of tissues" Texas City Rotary Club

(November 2, 1999).

1999 Invited Seminar and Exploratory Discussion "Thrombin Peptides to promote repair of acute dermal, bone, and cardiovascular injuries: potential application to the Mars Mission" NASA, Houston, TX (November 9, 1999).

1999 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" ConvaTec, Skillman, NJ (November 16-17).

2000 Presentation, "Thrombin peptide TP508 pre-clinical efficacy and Interim report on Diabetic Ulcer Trial DIAB001" Ross-Abbott, Coumbus Ohio (February 11, 2000).

2000 Invited Presentation "TP508 in Chronic Ulcers, Interim Data Diabetic Ulcer Trial DIAB001 and plans for international marketing" Abbott Laboratories (March 9, 2000).

2000 Co-Organizer and Speaker, 1st International Certosa de Pontignani Symposium: Thrombin and Thrombin Peptides in Inflammation and Tissue Repair. Siena, IT (May 13-16, 2000).

2000 Meeting and Discussions with companies:
Wound Healing Society Toronto, Canada (June 3-6,2000)

2000 Meeting and Discussions with companies: American Diabetes Association Meeting meet with clinical trial site coordinators San Antonio, TX (June 9-11,2000).

2000 Meeting and Discussions with companies: Direct Myocardial Revascularization, Washington DC (Separate meetings to set up collaborations to revascularize ischemic heart with Baylor and MicroMed Technologies), (June 21-23, 2000).

2000 Civic Presentation, "Chrysalis and Chrysalin ®, update on developing pharmeceutical companies in Texas" Representative Patricia Gray, Galveston, TX. (July 13,2000).

2000 Writing workshop (European Grant), Siena IT (August 16-22).

2000 Orthopedic TP508 Workshop, Sun Valley Idaho (August 30-September 2, 2000).

2000 Presentation, "Potential of TP508 in myocardial revascularization and inhibition of restenotic lesions" Abbott Laboratories Cardiovascular Development Group. (September 21, 2000).

2000 Participant, Tissue Repair Symposium, Virginia Commonwealth University, Richmond VA. (September 25-26, 2000).

2000 Invited Corporate Presentation (Delivered by D McWilliams) SouthWest BioVentures Conference, Moody Gardens (December 6, 2000).

2001 Thrombin Peptide Molecular Biology Symposium, Tremont House, Galveston TX (January 11-13, 2001).

2001 Presentation, "Effect of TP508 on porcine wounds and Othropedic update" (joint meeting with Chrysalis, Abbott, and OrthoLogic, Philadelphia, PA, March 12, 2001).

2001 Presentation, "TP508 interaction with NPAR, Background related to novelty of prior discoveries" U.S. Patent Office, Washington, DC. (June 5, 2001).

2001 Invited Speaker and Session Leader, 6th International Meeting on Angiogenesis: Basic Science and Clinical Developments. "Tissue repair stimulated by the angiogenic thrombin peptide, TP508" Crete, Greece (June 26-July 2nd, 2001).

2001 Invited Speaker, 3rd Annual Conference on Angiogenesis: Innovative Science and New Applications. "Thrombin Peptide TP508: An Angiogenic Factor that Accelerates both Dermal Wound Healing and Fracture Repair." Boston, MA (July 31, 2001).

2001 Delegate, European Tissue Repair Society Conference. Wales, UK (September 3-7, 2001).

2001 Investigators Meeting "Results of Phase II Trial Effect of TP508 on Diabetic Ulcers (Chrysalis DIAB001), Tremont House Hotel, Galveston, TX (September 8, 2001).

2001 Presentation, "Effects of TP508 on Distal Radius Fracture Phase I/ II Trial (OrthoLogic)" FDA, Washington, DC (October 29, 2001).

2001 Invited Speaker & Roundtable Discussant, "Managing the Spinout Process: The Story of Chrysalis BioTechnology" SouthWest BioVenture Conference. Houston, TX (December 4-5, 2001).

2001 Four Poster Presentations, American Society for Cell Biology Annual Meeting, Washington DC (December 8-12, 2001).

BIBLIOGRAPHY

A. ARTICLES IN JOURNALS:

1. **Carney, D. H.** and Cunningham, D. D. Initiation of chick cell division by trypsin action at the cell surface. Nature 268: 602-666, 1977.

2. **Carney, D. H.**, Glenn, K. C. and Cunningham, D. D. Conditions which affect initiation of animal cell division by trypsin and thrombin. J. Cellular Physiol. 95:13-22, 1978.

3. Baker, J. B., Barsh, G. S., **Carney, D. H.** and Cunningham, D. D. Dexamethasone modulates the binding and action of epidermal growth factor in serum-free cell culture. Proc. Natl. Acad. Sci. USA 75:1882-1886, 1978.

4. **Carney, D. H.** and Cunningham, D. D. Cell surface action of thrombin is sufficient to initiate division of chick cells. Cell 14:811-823, 1978.

5. **Carney, D. H.** and Cunningham, D. D. Role of specific cell surface receptors in thrombin-stimulated cell division. Cell 15:1341-1349, 1978.

6. **Carney, D. H.** and Cunningham, D. D. Transmembrane action of thrombin initiates chick cell division. J. Supramol. Struct. 9:337-350, 1978.

7. **Carney, D. H.**, Glenn, K. C., Cunningham, D. D., Das, M., Fox, C. F. and Fenton, J. W., II. Photoaffinity labeling of a single receptor for alpha-thrombin on mouse embryo cells. J. Biol. Chem. 254:6244-6247, 1979.

8. Glenn, K. C., **Carney, D. H.**, Fenton, J. W., II and Cunningham, D. D. Thrombin active site regions required for fibroblast receptor binding and initiation of cell division. J. Biol. Chem. 255:6609-6616, 1980.

9. **Carney, D. H.** Visualization of thrombin receptors on mouse embryo fibroblasts using fluorescein-amine conjugated human-thrombin. J. Supramol. Struct. 13:467-478, 1980.

10. Crossin, K. L. and **Carney, D. H.** Evidence that microtubule depolymerization early in the cell cycle is sufficient to initiate DNA synthesis. Cell 23:61-71, 1981.

11. Crossin, K. L. and **Carney, D. H.** Microtubule stabilization by taxol inhibits initiation of DNA synthesis by thrombin and epidermal growth factor. Cell 27:341-350, 1981.

12. **Carney, D. H.** and Bergmann, J. S. ^{125}I-thrombin binds to clustered receptors on noncoated regions of mouse embryo cell surfaces. J. Cell Biol. 95:697-703, 1982.

13. Bergmann, J. S. and **Carney, D. H.** Receptor-bound thrombin is not internalized through coated pits in mouse embryo cells. J. Cell. Biochem. 20:805-817, 1982.

14. Stiernberg, J., LaBelle, E. F. and **Carney, D. H.** Demonstration of a late amiloride-sensitive event as a necessary step in initiation of DNA synthesis by thrombin. J. Cell. Physiol. 117:272-281, 1983.

15. **Carney, D. H.** Immunofluorescent visualization of specifically bound thrombin reveals cellular heterogeneity in number and density of thrombin receptors. J. Cell. Physiol. 117:297-303, 1983.

16. Thompson, W. C., Asai, D. J. and **Carney, D. H.** Heterogeneity among microtubules of the cytoplasmic microtubule complex detected by a monoclonal antibody to alpha tubulin. J. Cell. Biol. 98:1017-1025, 1984.

17. Stiernberg, J., **Carney, D. H.**, Fenton, J. W., II, and LaBelle, E. F. Initiation of DNA synthesis by human thrombin: Relationships between receptor binding, enzymic activity and stimulation of $^{86}Rb^{+}$ influx. J. Cell. Physiol. 120:289-295, 1984.

18. **Carney, D. H.**, Stiernberg, J. and Fenton, J. W., II. Initiation of proliferative events by human-thrombin requires both receptor binding and enzymic activity. J. Cell. Biochem. 26:181-195, 1984.

19. **Carney, D. H.**, Scott, D. L. and Gordon E. A. Phosphoinositides in mitogenesis: Neomycin inhibits thrombin-stimulated phosphoinositide turnover and initiation of cell proliferation. Cell 42:479-488, 1985.

20. Ball, R. L., **Carney, D. H.**, Albrecht, T. and Asai, D. J. and Thompson, W. C. A radiolabeled monoclonal antibody binding assay for cytoskeletal tubulin in cultured cells. J. Cell Biol. 103:1033-1041, 1986.

21. **Carney, D. H.**, Herbosa, G. J., Stiernberg, J., Bergmann, J. S., Gordon, E. A, Scott, D. and Fenton, J. W., II. Double signal hypothesis for thrombin initiation of cell proliferation. Seminars in Thrombosis Research 12:231-240, 1986.

22. Gordon, E. A and **Carney, D. H.** Thrombin receptor occupancy initiates cell proliferation in the presence of phorbol myristic acetate. Biochem. Biophys. Res. Comm. 141:650-656, 1986.

23. Frost, G. H., Thompson, W. C. and **Carney, D. H.** Monoclonal Antibody to the Thrombin Receptor Stimulates DNA Synthesis in Combination with Gamma-Thrombin or Phorbol Myristate Acetate. Journal of Cell Biology 105:2551-2558, 1988.

24. Glenn, K. C., Frost, G. J. Bergmann, J. S. and **Carney, D.H.** Synthetic peptides representing the thrombin-receptor binding domain bind to high-affinity thrombin receptors on fibroblasts and modulate thrombin mitogenesis. J. Peptide Research 1: 65-73 1989.

25. Ball, R.L., **Carney, D.H.** and Albrecht, T. Taxol inhibits stimulation of cell DNA synthesis by human cytomegalovirus. Experimental Cell Research 191:37-44. 1990.

26. Frost, G. H., Bergmann, J.S., and **Carney D.H.** Glycosylation of high-affinity thrombin receptors appears necessary for thrombin binding. Biochem. Biophys, Res. Comm. 180:349-355, 1991.

27. Hokanson, J.A., Hayward, P.G., **Carney, D.H.**, Phillips, L.G. and Robson, M.C. Mathematical models, life table methods, and the analysis of experimental wound healing data. Wounds 3: 213-220. 1991.

28. Belloni, P.N., **Carney, D.H.** and Nicolson, G.L. Isolation and partial characterization of murine and human endothelial cells from various organs: Differential responsiveness to thrombin and other growth factors. Microvascular Research 43 (1): 20-45, 1992.

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